[Poster Board # F24] Cigarette Smoking Affects Alveolar Macrophage Function In Vitamin D Deficient And Vitamin D Sufficient Mice, [Publication Page: A4847]

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Rationale

Chronic obstructive pulmonary disease (COPD) is associated with a defective alveolar macrophage function. COPD patients often exhibit vitamin D (vitD) deficiency, which correlates with disease severity. Both cigarette smoke and vitD are known to modulate important antimicrobial functions of alveolar macrophages. In the present study we investigated the combined effect of cigarette smoking and vitD deficiency on alveolar macrophage function and disease progression in a mouse model of COPD.

Methods

VitD deficient (n=23) or sufficient (n=18) male C57Bl/6 mice of 8 weeks old were daily exposed to cigarette smoke or ambient air using a nose-only exposure system (Scireq). After 6 weeks of smoking, lung function was determined with whole-body plethysmography (Buxco Maneuver system). The cellular composition of the bronchoalveolar lavage (BAL) fluid was assessed with Fluorescence Activated Cell Sorting (FACS) and cytospin. Macrophage function was evaluated by testing the ability of airway CD11c+CD11blow cells to phagocytose and to produce reactive oxygen species (oxidative burst capacity) following interaction with *E. coli* bacteria.

Results

Analysis of the lung function following a 6-week smoking interval revealed a slight trend towards hyperinflation of the lungs with increased total lung capacity (TLC) and compliance compared with the air-exposed groups (Table 1). Smoke exposure was associated with a prominent neutrophilic inflammation and CD4+- and CD8+ T cell infiltration in the airways, while slightly lower levels of CD11c+CD11blow macrophages were observed. Moreover, smoking resulted in a significant reduction of CD11c+CD11blow macrophages to phagocytose and initiate an oxidative burst response following bacterial interaction when compared to air-exposed mice (Table 1). However, neither the cellular composition of the airways nor macrophage phagocytic- and oxidative burst functions were significantly different between vitD deficient and vitD sufficient mice.

Conclusion

Our results confirm a strong association of cigarette smoke exposure and decreased alveolar macrophage phagocytic- and oxidative burst capacity. VitD deficiency did not aggravate smoke-induced functional defects of alveolar macrophages or COPD disease progression. As 3 months of cigarette smoke exposure are minimally required to induce emphysema, differences may become only apparent after a more prolonged period of cigarette smoking and vitD deficiency.

		Lung function		Phagocytosis	Oxidative burst
		TLC (mL)	Compliance (mL/cmH2O)	(%)	(%)
VitD	Air-				

sufficient	exposed	0.92±0.11	0.051±0.007	40±5.3	39±2.3
	Smoking	1.05±0.12	0.057±0.006	11±5.2	18±5.8
VitD deficient	Air-exposed	0.78±0.22	0.041±0.01	54±12.1	48±12
	Smoking	0.95±0.13	0.051±0.008	13±3.91	18±4.9

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